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Asthma and Hay Fever

Studies on Antibodies to Yeasts in Bronchial Asthma. Goldin, M., Libretti, A., Hoffman, A., and Kaplan, M. A.: Ann. Allergy **15**: 119, 1957.

The etiologic significance of *Candida (Monilia) albicans* and *Geotrichum* in bronchial asthma was evaluated on the basis of agglutinin titers, skin tests, and the gel diffusion technique. The sera of rabbits immunized with *Candida albicans, Candida krusei, Saccharomyces cerevisiae,* and *Geotrichum* were tested for their antibody titer against homologous and heterologous boiled yeast cell suspensions and against sheep cells sensitized with the alcohol-insoluble fraction of each of the yeast cells. Agglutinins against each of the yeasts were demonstrated but the hemagglutination technique proved to be more specific than the yeast cell technique. In order to establish whether antibodies in the yeast might be of the "incomplete" or "blocking" type, the yeast cells which had previously reacted with their specific antisera were suspended in guinea pig anti-rabbit globulin sera and in several other diluents, including human

type AB serum, and the same procedures were repeated with the sensitized sheep red cells. No significant increase in the agglutinin titers was observed with this technique.

The gel diffusion technique demonstrated bands of precipitate with homologous but not with heterologous alcohol-insoluble antigens. Absorption of the antiserum by homologous yeast cell suspensions resulted in the disappearance of the precipitate bands, whereas absorption with heterologous antigens did not affect the bands of precipitate. No precipitate occurred when the alcohol-soluble fraction was used.

The sera of 20 patients with chronic bronchial asthma of unknown etiology, each of whom had had *C. albicans* isolated from his sputum, and the sera of 20 normal individuals were examined for their agglutination titer by the above procedures. The results demonstrated that antibodies to yeast occur commonly in both asthmatic and normal individuals in the same degree and at comparable titer levels. It was also shown that these antibodies were not "incomplete" or "blocking" in nature. The gel diffusion technique failed to produce any bands of precipitate with human sera.

Intracutaneous skin tests were performed with various dilutions of yeast extracts prepared from the alcohol-insoluble and the alcohol-soluble fractions. No significant differences were noted between the skin reactions manifested by patients from whose sputum *C. albicans* had been isolated and the reactions manifested by the normal controls. H. F.

Effect of a City on the Fall-Out of Pollens and Molds. Implications for Civil Defense. Heise, H. A., and Heise, E. R.: J. A. M. A. **163**: 803, 1957.

Ragweed pollen and alternaria spore counts were made in the air above and about a city on the west shore of Lake Michigan. Microscopic slides coated with petrolatum were held in position mechanically near the ventilator of an airplane for 10-minute periods. Exposures were made at altitudes of 1,000 feet and 2,000 feet above the terrain. A typical report of a survey taken at 5:10 A.M. on Aug. 22, 1954, includes the following data: wind was about 8 miles per hour; the temperature on the ground was 65° F. and at 1,000 feet was 68° F.; the dew point was 60° F.

Pollen counts at altitudes of 1,000 and 2,000 feet, respectively, were as follows: over the city, 550 and 162; south of the city, on the "country" or windward side, 925 and 280; north of the city, 75 and 105; west of the city, 70 and 150; east of the city, 90 and 110. A similar relationship between counts over the city and its periphery was noted for alternaria spores. The fact that higher counts were generally obtained at 1,000 feet than at 2,000 feet reflected a "temperature inversion" phenomenon in that the air was cooler at lower than at higher levels, a condition favorable for fall-out. The counts were greatest on the windward side (south) and least on the leeward side (north and west) of the city. These differences were ascribed to the temperature differences between the city and the country and were attributed to the effects of rising currents of warmer air over the city, which have their greatest effect on the leeward side. It would seem, therefore, that a city should be safer from atomic fall-out, especially on the leeward side, than the surrounding country. M. C.

Intermittent Positive-Pressure Breathing-Aerosol Therapy for Asthma in Children. Goddard, R. F., and Roorbach, M. S.: J. A. M. A. **163**: 1125, 1957.

One hundred asthmatic children, from 1 to 17 years of age, were treated over a 4-year period with intermittent positive-pressure breathing-aerosol

therapy. Aerosol medication consisted of bronchodilators, antibiotics, or surface-active or mucus dissolving agents. Inspiratory pressures from 10 to 15 cm. H_2O were applied through a closely-fitting face mask; oxygen was used for pressure and for nebulizing the medication. Therapy optimally began with two to three treatments daily, followed by a gradual reduction in the number of applications to one each week and finally to periodic booster treatments several weeks apart. Supportive therapy, when indicated, included specific desensitization, immunizing injections for colds, antihistamines, diet control, rest, elimination of environmental offenders, psychotherapy, and antibiotics. Favorable results were reported in 98 per cent of the children as judged by subjective and objective signs of improvement, including routine laboratory studies and specific pulmonary function tests. H. Stryker.

Antigen-Antihistamine Mixtures in the Treatment of Highly Sensitive Pollen Patients. Sternberg, L.: New York J. Med. **57**: 2069, 1957.

The combination of antihistaminic drugs with pollen extracts to achieve higher dosage in the treatment of extremely sensitive pollen cases is decried. In the author's experience, most patients are able to take a definite dose of pollen extract with safety. Raising this dose rarely improves the clinical result and usually causes severe local or general reactions. Unquestionably, some of the minor reactions may be avoided by administering antihistamines with pollen doage. Severe constitutional reactions, however, are not prevented by this procedure.

Most of the reports which stress the advantages of increasing dosage of pollen extracts in highly sensitive cases by means of the addition of antihistaminic drugs fail to take into account the fact that clinical results are not dependent solely on the dose attained. Furthermore, the clinical improvement attributed to increased dosage may be accounted for by the pharmacologic effects of the added antihistaminic drug. M. A.

Enzyme Therapy by Intramuscular Route in Chest Diseases. Silbert, N. E.: Dis. Chest **29**: 520, 1956.

Trypsin in doses of 2.5 mg. dissolved in sesame oil was administered intramuscularly once a day to 24 patients with bronchial asthma. These injections were given daily for 5 to 7 days, then every second or third day for 2 weeks, and the last dose a week later. There were 23 adults and one 9-year-old child in the group. Asthma in most cases was persistent and severe, and in 10 patients it was associated with chronic bronchitis. Seven of the patients were given a second course of treatment, and 5 received a third course. Radiological examinations of the patients prior to therapy showed varying degrees of localized or generalized emphysema, increases in the width and density of hilar shadows, and increases in the bronchovascular markings with streak-like shadows in both bases. In 10 cases, a honeycomb pattern with finger-like, dense projections extending from the lung roots with irregular areas of radiolucency was felt to be evidence of bronchiectasis. No bronchoscopic examinations were reported.

Subjectively, all patients found it easier to raise sputum after one to three days and all felt better after the first course of injections. The improvement in symptoms lasted from 10 days to 6 months. Six of 7 patients who received a second course were improved. One patient had an exacerbation of asthma during the second course. Posttreatment x-rays indicated marked

improvement in 13, slight or moderate improvement in 9, and no improvement in 3. Side effects mentioned included pain at the site of the injection, fine maculopapular rashes about the pelvis, and dizziness. E. W.

Obstruction of Large Portions of the Lungs in Bronchial Asthma. VanGeuns, H. A.: Nederl. tijdschr. geneesk. **100**: 3702, 1956.

Three patients with bronchial asthma complicated by chronic bronchitis were found to have occlusions of large bronchial segments with mucus plugs. In one patient, the middle lobe bronchus and several bronchi of the basal segments of the right lung were occluded. In another, the upper three segments of the left upper lobe were occluded. In the third patient, the left upper lobe was involved. Treatment in each case consisted of bronchoscopic aspiration of the mucus plugs which resulted in marked improvement. Following bronchoscopy, the patients were able to cough up much viscous sputum. M. C.

Dermatology

Racial and Environmental Factors in Susceptibility to Rhus. Epstein, E., and Claiborne, E. R.: Arch. Dermat. **75**: 197, 1957.

A review of the case histories of 12,000 private patients revealed an incidence of 2.8 per cent of Rhus dermatitis. Of the entire group about 85 per cent were Caucasians, 11 per cent were Negroes, and 4 per cent were Orientals. The incidence of dermatitis according to race was 3.2 per cent among the whites and 0.9 per cent among the Negroes. There were no cases of Rhus dermatitis among the Orientals. Another study of the incidence of Rhus dermatitis conducted in two large college infirmaries where there was a high census of Oriental students showed that of 184 cases of Rhus dermatitis only 0.5 per cent occurred in Orientals born in this country and only 0.17 per cent occurred in foreign-born Orientals.

A group of 900 patients were patch tested with dilutions of Rhus toxin ranging from 1:10 to 1:1,000. The tests were read in 24 to 48 hours. Positive reactions were obtained only with the 1:10 dilution. About 40 per cent of the white and Negro patients and about 70 per cent of the Orientals reported previous exposure to some member of the Rhus group. The incidence of positive reactions was 31 per cent among the Caucasians, from 18 per cent to 28 per cent among the American-born Orientals, and from 1 to 3 per cent among foreign-born Orientals. No positive reactions were encountered among 34 foreign-born Filipinos. From 17 to 23 per cent of the whites and Negroes and from 5 to 18 per cent of the Orientals reported that they had had Rhus dermatitis at some time in the past. The incidence of Rhus dermatitis among the American-born Orientals was similar to that of the whites and Negroes, while the incidence among the Orientals born overseas was only 0.17 per cent.

Since there is no appreciable difference in susceptibility among the racial groups born in this country, pigmentation and other racial characteristics are not factors in protection against the Rhus group. However, environmental factors may be important in producing protection. Since the mango tree of Hawaii and the lacquer plants of the Orient are such potent immunizers and are members of the Rhus family, the authors postulate that exposure to these plants may be the source of protection for the Orientals born overseas. It is further suggested that extracts of mango or lacquer plants may be useful prophylactically in producing immunity to poison oak or poison ivy. R. W.

Physiologic Studies in Atopic Dermatitis (Disseminated Neurodermatitis). II. The Effect of Denervation on the "Delayed Blanch Phenomenon." Lobitz, W. C., Jr., Heller, M. L., and Dobson, R. L.: Arch. Dermat. **75**: 228, 1957.

In a previous article, the authors noted that patients with atopic dermatitis respond to the intracutaneous injection of acetylcholine (1:10,000 and 1:100,000) with a "delayed blanch phenomenon" or vasoconstriction instead of with the normal response of vasodilatation. To investigate the possible causes for this response, patients with atopic dermatitis were submitted to the following types of skin denervation: "(1) local intradermal infiltration of the skin with a solution of 1% procaine hydrochloride in buffered isotonic saline solution; (2) a 'field block' of the skin with 1% procaine hydrochloride solution; (3) the injection of a 1% procaine hydrochloride solution intravenously; (4) a brachial plexus nerve block; and (5) a unilateral lumbar sympathectomy."

None of the techniques of denervation altered the "delayed blanch phenomenon" produced by the intracutaneous injection of acetylcholine. The authors concluded that denervation does not influence the "delayed blanch phenomenon" which occurs in patients with atopic dermatitis following the intracutaneous injection of acetylcholine. R. W.

Specific Tests and Treatment of Eczema Solaris. De los Santos, J.: Med. latina de la Habana **15**: 121, 1956.

Light is a combination of chemical and physical energy which produces allergic and nonallergic photosensitivity. The allergic type includes reaginic and nonreaginic mechanisms. While the localization of symptoms to areas exposed to the sun's rays aids in the diagnosis, it must be remembered that lesions may be present even in places protected by clothes and that other types of eczema may also appear on the areas exposed to the sun. Several case histories are presented.

Specific tests were made by covering the skin with a dark material in which there was a small opening for exposure of the skin to the sun's rays. After it has been proved that sun sensitivity exists it is helpful to determine which part of the spectrum is the offender. Other allergic tests and studies, suggested by the patient's history, should be made.

The photosensitizing agents operative in each case should be sought. Among those commonly found are oil products, sulfonamides, liquors (cognac) or foods, hydrochloric acid, and many other substances.

In the symptomatic treatment, ACTH and the new cortisone compounds have been used successfully. The patient should be protected from direct or indirect exposure to the sun's rays. Recommended for use are ethylenediamine ointment, nicotinic acid, resorcin, sodium hyposulfite, pyrocatechin by mouth, quartz light for the patient who has no sensitivity to ultraviolet rays, and quinacrine. J. C.

Contact Dermatitis to Hydrocortisone Ointment. Sama, W. M.: J. A. M. A. **164**: 11, 1957.

A case is reported in which the local use of 1 per cent hydrocortisone ointment as part of the treatment of a leg ulcer resulted in a severe eczematous skin eruption which involved the area under treatment and later the hands, forearms, face, and neck. Patch tests with the ointment were positive on two separate occasions in the same patient.

Hydrocortisone and the ingredients of the ointment base were tested individually. The sensitizing materials were found to be the free and sulfated high alcohols. The presence of hydrocortisone in the ointment did not prevent the reaction. The offending agents, especially sodium lauryl sulfate are widely used in detergents and skin preparations. H. Stryker.

Cutaneous Sensitivity Reactions to Chlorpromazine. Mullins, J. F., Cohen, I. M., and Farrington, E. S.: J. A. M. A. **162**: 946, 1956.

Cutaneous symptoms developed in 85 patients who were being treated with chlorpromazine. Generalized skin reactions occurring in 57 patients included morbilliform lesions, urticaria, seborrhea, purpura, papules, bullae, and miliaria-like lesions. There were 18 patients who developed erythematous papulovesicles as a result of photosensitivity. These lesions appeared only at sites that were exposed to sunlight and occurred predominantly during the summer season. The remaining 10 patients devloped typical eczematous dermatitis. Except for lesions produced by photosensitivity, doses of chlorpromazine greater than 400 mg. per day were required to produce skin reactions in the majority of cases. When the use of the drug was discontinued the lesions cleared rapidly. The medication could then be administered in smaller dosage without recurrence of the skin reactions. M. C.

Miscellaneous Allergies

Focal Encephalopathy After Administration of Tetanus Antitoxin. Poser, C. M.: J. A. M. A. **164**: 871, 1957.

A case of focal encephalopathy following tetanus antitoxin administration is reported. The patient was a 41-year-old woman who received 1,500 units of tetanus antitoxin after showing a negative reaction to a skin test with this material. She gave a history of an allergic reaction to an injection of penicillin about one year previously and had "asthma" every spring associated with "sinus trouble." A few days after the TAT injection the patient developed serum sickness, followed by symptoms of left hemiparesis and hemisensory defect superimposed on what appeared to be a diffuse encephalomyelitis. Treatment with ACTH and cortisone apparently helped to bring about a partial recovery.

The author points out the rarity of focal brain lesions in serum sickness. There are said to be only 11 cases with focal type cerebral complication of serum sickness in the literature. The cases were all characterized by a rather sudden onset of hemiplegia accompanied by confusion, coma, or convulsions. These clinical manifestations were attributed to a lesion resulting from vascular occlusion or insufficiency. As an explanation for the vascular lesion, it is suggested that the collagen tissue of the media of the arterial wall is the site of an antigen-antibody reaction. Injury to the endothelium and media may result in edema, which may occlude the vessel or impair circulation through it, or lead to increased permeability and even necrosis of the vessel wall. T. Chao.

Allergenicity of Tranquilizing Drugs. Bernstein, C., and Klotz, S. D.: J. A. M. A. **163**: 930, 1957.

The widespread use of tranquilizing drugs has resulted in a variety of reactions. Sensitization to reserpine has not been reported. Most reactions to this drug, such as flushing, nasal congestion, malaise, and urticaria, may be attributed to side effects of a histamine-like nature. There were 7 major

groups of side effects of chlorpromazine. These included nasal congestion, dermatitis, photosensitivity, pruritus, an influenza-like syndrome, agranulocytosis, and jaundice. The dermatitis consisted of a maculopapular, erythematous, pruritic eruption which characteristically involved the trunk and extremities and spared the face, palms, soles, and mucous membrane. Local lesions involving the anus and genitals and eczematous contact dermatitis also were noted. Jaundice developed after the first week of therapy in approximately 1 per cent of patients and was attributed to bile stasis with little or no inflammation. In rare cases of jaundice, a peripheral blood eosinophilia occurred which, when present, distinguished chlorpromazine jaundice from true obstruction jaundice. Meprobamate produced urticaria, angioedema, fever, arthralgia, and purpura. It was suggested that prior treatment with mephenesin may "presensitize" patients to Meprobamate. M. C.

The Treatment of Headache. Friedman, A. P., and Merritt, H. H.: J. A. M. A. **163**: 1111, 1957.

The results of studies to determine the effectiveness of various chemical agents in the treatment of chronic headache were summarized. Over 5,000 unselected subjects had each been given a placebo and two therapeutic agents in random order. Their subjective response was the chief criterion for evaluation. The drugs employed included analgesics, sedatives, anticonvulsants, central nervous system stimulants, vasodilators and vasoconstrictors, histamine and antihistamine, diuretics, vitamins, hormones, and drugs acting on the autonomic nervous system. The specific headache entities given special attention were migraine, headache due to tension, and headache due to hypertension.

The authors believe that migraine is best treated with a combination of ergotamine tartrate and caffeine. However, in a limited number of cases associated with or secondary to allergic manifestations, epinephrine or its derivatives may be of value. In those instances in which disorders of the nasal passages are present, the local application of vasoconstrictive agents frequently provides relief. The results of antihistamine therapy in chronic headache associated with allergy are inconclusive. H. Stryker.

Anaphylactic Reactions to Penicillin: Case Reports With Certain Immunologic Observations. Peters, G. A., Henderson, L. L., and Prickman, L. E.: Ann. Allergy **15**: 135, 1957.

Immunologic studies in 3 cases of severe nonfatal reactions to penicillin are presented. In one case, the patient on two occasions experienced loss of consciousness and cyanosis with feeble pulse and respirations shortly after the ingestion of penicillin tablets. A patch test performed with penicillin G showed no local reaction, but the patient experienced weakness, generalized warmth, prickling of the tongue, and pounding of the heart shortly after the patch was applied. Scratch tests with penicillin G performed first with a solution containing 20,000 U. per milliliter and then with one containing 5,000 U. per milliliter each showed marked local reactions plus the same pattern of systemic symptoms which followed the application of the patch test.

The other two cases reacted strongly to scratch and intradermal tests with penicillin G and gave positive passive transfer reactions. Penicillin O and penicillin V also gave positive passive transfer reactions but they were not so large as those evoked with penicillin G. When the sera of these patients were heated to 56° C. for 4 hours, they lost their capacity to sensitize normal skin passively. An attempt to sensitize guinea pigs passively with the sera of the penicillin-reactive patients proved unsuccessful.

The authors believe that skin testing with penicillin is sufficiently reliable to warrant its use, particularly in atopic individuals, prior to the administration of penicillin. If the reaction to the test is positive, penicillin therapy should be avoided. H. F.

Apnea Due to Benadryl. Brody, J. I., and Tobin, J. L.: Ann. Int. Med. **47**: 172, 1957.

A nurse with hay fever took 50 mg. of Demerol orally at 6:30 A.M., 100 mg. of Benadryl at 9:00 A.M., and 100 mg. more of Benadryl at 10:30 A.M. At approximately 11:00 A.M. she was found on the floor of the hospital in an apneic condition. Manual artificial and then mechanical respirations were given for 10 minutes, following which the patient began to breathe on her own. She began to speak incoherently about 30 minutes after the initial episode, and then slept for some five hours. No medications were given. Examination was negative except for hyperactive deep tendon reflexes and ankle clonus. The patient was discharged to duty the next day. This case was considered to be of particular interest because there have been no reports of Benadryl intoxication where apnea has been the initial clinical manifestation. A review of the literature revealed that Benadryl causes two main toxic reactions: that of depression, seen mostly in adults, and that of stimulation, seen mostly in infants and children and manifested by convulsions. The Demerol which the patient had taken was considered to have been insufficient to cause respiratory depression, although it may have potentiated the action of the Benadryl.
M. C.

Combined Hypersensitivity Reaction to Sodium Para-Aminosalicylate and Associated Antibacterial Drug Concurrently Administered. Cohen, A. A., and Lawrence, S. H.: Ann. Int. Med. **46**: 893, 1957.

A 32-year-old physician with a 1 cm. nodule in the right lung was given 100 mg. of isoniazid and 4 grams of PAS three times daily. On the twenty-sixth day he noticed leg pains, chills, and fever and his temperature rose to 103.2° F. Physical examination showed redness of the throat, enlarged lymph nodes, a scarlatiniform rash, and a palpable liver and spleen. There was relative lymphocytosis, and atypical lymphocytes were seen. All medication was discontinued and within 24 hours he was asymptomatic. After one week, combined therapy was started again and within 2 hours a chill and a temperature of 104° developed. Three days later, 100 mg. of INH alone was given and again fever and chills occurred. Finally 3 days later, 4 grams PAS were given alone and again a similar reaction followed. The patient was subsequently given streptomycin alone, with no ill effects. The heterophile antibody titer was not elevated. Two similar cases were also described. The 3 cases demonstrated the development of an infectious mononucleosis-like syndrome to PAS. Two of them exhibited an additional phenomenon, the reproduction of a similar clinical picture following a test dose of INH. The mechanism of the reactions was not known, although evidence was presented in favor of a specific allergic sensitivity to the offending drugs. M. C.

Bilateral Allergic Neuronitis of the Acoustic Nerve After Administration of Tetanus Antitoxin. Thomas, J. E., Goldstein, N. P., and Williams, H. L.: Proc. Staff Meet., Mayo Clin. **32**: 131, 1957.

A 35-year-old female developed serum sickness within 24 hours following the administration of 1,500 units of tetanus antitoxin which was given because

of a finger laceration. Seven days after the injection of antitoxin the patient experienced distortion of sounds and roaring in the ears. The next morning she was deaf. Tinnitus, dizziness, and some loss of the senses of smell and taste followed. Audiometric testing revealed bilateral symmetrical loss of perception. The functions of the labyrinths were reduced on both sides. After 5 months, partial improvement had taken place. The diagnosis was that of an allergic cochlear vestibular neuronitis secondary to serum sickness following the administration of tetanus antitoxin. M. C.

Treatment of Anaphylactic Drug Reaction. Clinical Anesthesia Conference: New York J. Med. **56**: 3739, 1956.

A severe anaphylactoid reaction associated with cardiovascular collapse followed an intravenous injection of a contrast medium in a 35-year-old male Negro. The patient received 30 c.c. of contrast medium intravenously for a pyelogram. During the injection he became nauseated and vomited. Within 15 minutes after the injection was completed, his face became puffy and he collapsed. His breathing became labored. His pulse could hardly be palpated and the blood pressure could not be obtained. The resident immediately began an intravenous infusion of 5 per cent dextrose in water and then administered 10 mg. of Chlor-Trimeton intravenously, followed immediately by 0.5 mg. of Adrenalin. Improvement started about 10 minutes later, when the patient began to respond to questions and the carotid pulse was discernible. At this time, the pulse rate was 50 and the blood pressure was 60/40. The patient's legs were elevated and 4 mg. of d-desoxy-ephedrine was injected intravenously. Within 5 minutes the blood pressure rose to 76/50 and with an additional 4 mg. of d-desoxy-ephedrine it rose to 100/70. The pulse rate was 60 per minute and was irregular. An electrocardiogram showed an irregular irregularity, read as flutter fibrillation associated with a variable heart block. At the sixth hour the blood pressure suddenly began to fall and a continuous infusion of 0.1 per cent Neo-Synephrine was begun and continued for 6 hours. Within 12 hours after the initial symptoms all signs of allergic manifestation had disappeared and within 36 hours normal sinus rhythm suddenly developed.

It is pointed out that, although treatment was prompt and the proper kinds of drugs were used, the dosage was excessive and injudicious. The cardiac irregularity may have been induced by the intravenous injection of Adrenalin. The rapid injection of the Chlor-Trimeton was also a questionable procedure. M. A.

Simultaneous Hypersensitivity to Streptomycin and Para-Aminosalicylic Acid. Report of Two Cases. Silverman, J. D., Swenson, E. W., and Gray, J. A.: Dis. Chest. **30**: 103, 1956.

The development of simultaneous hypersensitivity to streptomycin and para-aminosalicylic acid in 2 patients with pulmonary tuberculosis was reported. In the first patient, a 2-year-old child with a positive family history of allergy, fever, exfoliation, tender lymphoglandular enlargement, and hepatosphenomegaly developed 26 days after the start of chemotherapy. Leukocytosis with 16 per cent eosinophilia, toxic granulation of the neutrophiles, hypoalbuminemia, hyperglobulinemia, and the presence of albumin, erythrocytes, and casts in the urine were other manifestations. There was also evidence of mild liver dysfunction. Treatment with ACTH cleared the condition

within 5 weeks. The administration of streptomycin or para-aminosalicylic acid separately produced a rash, fever, and leukocytosis with eosinophilia.

In the second patient, a 41-year-old Negro with pulmonary tuberculosis, exfoliation, leukocytosis, eosinophilia, generalized lymph gland enlargement, and lymphocytosis in the spinal fluid began to develop 41 days after the initiation of chemotherapy. After recovery, the administration of either para-aminosalicylic acid or streptomycin produced a fever and a 25 per cent eosinophilia within 3 hours. E. W.

Anaphylaxis

Effect of Temperature on the Anaphylactic Reaction. Mongar, J. L., and Schild, H. O.: J. Physiol. **135**: 320, 1957.

The anaphylactic responses of sensitized guinea pig organs were studied with the Dale technique. The amount of histamine released was assayed on guinea pig ileum. When sensitized lung tissue was exposed to elevated temperatures for 25 minutes, there was no evidence of inactivation below 42° C. At 43° C., heat inactivation was incomplete and the anaphylactic mechanism gradually returned in about 6 hours. At 45° C., however, inactivation was complete. Lowering the pH of the tissue to 6.4 made heat inactivation at 42.5° C. more complete. Changes of pH in the range of 7.5 to 8.4 had no noticeable effect on heat inactivation. Temperatures which inactivated the anaphylactic mechanism also affected the contractile function of the normal muscle cell, but only as long as the preparation was kept at the higher temperature.

Once the histamine release mechanism had been inactivated by heating, it could not be appreciably restored by 90-minute incubation with antibody so it was not possible to resensitize passively a sensitized tissue which had been previously heated. It was also impossible to sensitize passively normal heated lung tissue. However, these preparations could still respond to histamine, showing that their contractility was undamaged by the heat treatment.

Low temperatures were also found to inhibit anaphylaxis. Cold inhibited not only histamine release, but also desensitization. At 17° C. the histamine release was completely inhibited, while desensitization was only slowed down. The effect of cold differed from that of heat, however, in that it produced no permanent effects. Thus, when a sensitized tissue had been cooled to 7° C. for periods of up to one hour and then brought back to 37° C., a normal amount of histamine was released following exposure to antigen. The inhibition of histamine release by antigen was seen only when the antigen was added in the cold.

It is suggested that heating inactivates a tissue component, such as the precursor of an enzyme, which is required in the anaphylactic reaction. This heat-labile component is presumably a protein but is not complement. In summation, the authors state that the effect of heat on the anaphylactic response of isolated tissues was not entirely reversible and that the less complete was the inactivation, the greater was the chance of recovery. The authors theorize that in anaphylaxis antigen combines with antibody, resulting in the activation of an enzyme system which starts reactions leading to histamine release and the other effects of anaphylaxis. The activated enzyme has a brief existence and becomes rapidly inactivated. Physical factors and chemicals which interfere with the anaphylactic reaction probably do so by their action on the enzyme mechanism. R. W.

Effect of Allergic Shock on Fate of Staphylococci in the Organs of Mice. Prigal, S. J., and Dubos, R. J.: Proc. Soc. Exper. Biol. & Med. **93**: 340, 1956.

The ability of two different breeds of pertussis-vaccinated mice to develop an anaphylactic type of sensitization to bovine serum was demonstrated. The reaction was considered specific since there were no deaths among animals pretreated only with pertussis vaccine and challenged with bovine serum or among animals sensitized with bovine serum and pertussis vaccine and challenged with rabbit serum or egg albumin.

Groups of mice were pretreated by the intraperitoneal injection of bovine serum and pertussis vaccine or by the injection of pertussis vaccine alone. From 10 to 23 days later, they were injected intravenously with staphylococci suspended in $\frac{1}{2,000}$ bovine serum and were sacrificed 24 hours later. Regardless of the interval between sensitization and infection, more staphylococcal colonies were recovered from the kidneys, livers, and lungs of animals that had been sensitized to bovine serum than from the organs of control animals. The authors suggest that the severity of the infectious process had been increased in the bovine-serum-sensitized animals by the mild allergic shock resulting from the injection of bovine serum in the diluent for the staphylococcal suspension. B. S.

Alteration of Plasma Electrophoretic Patterns and Anaphylactic Reactions in Protein Depleted Dogs. Hahn, P. F., Baugh, P., and Meng, H. C.: Proc. Soc. Exper. Biol. & Med. **93**: 448, 1956.

Eight dogs were depleted of protein for 6 months by forcing hemoglobin production. The dogs were maintained at an anemic level by repeated bleedings, and colloidal iron was administered intravenously in amounts sufficient to ensure the existence of an excess in stores at all times. In addition to these measures, the animals were kept on diets highly restricted in their protein content. Eleven healthy, well-fed dogs were used as controls.

The depleted and control dogs were sensitized with horse serum by intravenous and subcutaneous injections. After 3 weeks, they were challenged with an intravenous injection of horse serum. All 11 control animals exhibited the usual symptoms of anaphylaxis, with the exception of one which manifested excessive itching only. Two of these dogs died within 12 hours. The depleted animals exhibited milder anaphylactic manifestations or none at all, and none died.

Plasma electrophoretic studies were done before and after the depletion period. The total plasma proteins showed an average reduction of about 20 per cent. This relatively small change was in marked contrast to the decrease in A/G ratio from an average of 0.83 in the control group to 0.12 in the depleted group, a decrease of about 85 per cent. The percentage of albumin varied from 40 to 50 per cent under normal conditions and was reduced to from 9 to 13 per cent in the depleted state. The total α-globulins were increased in each depleted animal, as were the beta-1 and beta-2 globulins. The values for gamma globulin were approximately doubled in the depleted state. If the anaphylactic-antibody-containing globulin fraction was decreased in the depleted animals, this could not be detected in the above studies. Increases in other components of the gamma and beta-2 globulin fractions may have masked the reduction of this antibody-containing fraction. B. S.

Pharmacology, Physiology, and Pathology

Conversion of C^{14}-Arterenol to Epinephrine in Vivo. Masuoka, D. T., Schott, H. F., Akawie, R. I., and Clark, W. G.: Proc. Soc. Exper. Biol. & Med. **93**: 5, 1956.

Four rats were injected intraperitoneally with α-C^{14}-dl-arterenol hydrochloride twice daily for 3 days and were sacrificed 24 hours after the last injection. Six other rats were given 6 hourly injections of this substance and were sacrificed one hour after the last injection. The adrenal glands of all rats were removed and ground into a suspension with acetic acid. The adrenal suspensions were studied by paper chromatography and an isotope dilution method. With both methods, C^{14}-epinephrine was found in all adrenal glands, indicating that the α-C^{14}-arterenol was converted to adrenal epinephrine. These studies represent the first direct evidence that arterenol is converted to epinephrine. This evidence completes the postulated reaction sequence which leads from phenylalanine to epinephrine. B. S.

Influence on Circulating 17-Hydroxycorticosteroid Concentrations of Compounds Structurally Related to Salicylate. Done, A. K., Ely, R. S., and Kelley, V. C.: Proc. Soc. Exper. Biol. & Med. **93**: 294, 1956.

Guinea pigs were injected intraperitoneally with equimolar doses of the sodium salts of 25 different benzoic acid derivatives. Four hours later, the animals were bled and the plasma concentration of 17-hydroxycorticosteroid was determined. Benzoic acid had no effect on the plasma 17-OHCS concentration. Animals given o-hydroxybenzoic (salicylic) acid showed a significant elevation of the plasma steroid. In contrast, m- or p-hydroxybenzoic acid had no significant effect. The o-substituted methoxy and ethoxy derivatives were found to be active in producing elevated 17-OHCS concentrations. Questionable activity or none at all was found with the m- and p-methoxy and with p-ethoxy derivatives. On the other hand, 3,4,5-trimethoxybenzoic acid produced highly significant elevations. The amino derivatives of benzoic acid were relatively inactive. The addition to the salicylate structure of another hydroxyl group in the 3 or 6 position or of an ether group in the 3 position resulted in increased activity. Acetylsalicylic acid exerted the greatest effect on plasma 17-OHCS concentration of any of the compounds tested. Salicyluric acid, the principal salicylate metabolite, had no effect.

In general, there seems to be a good correlation between the reported antirheumatic potency of some of the above compounds and their ability to produce elevated circulating corticosteroid concentrations. However, numerous discrepancies appear to exist between the adrenal ascorbic acid depleting ability of these drugs and either their antirheumatic effects or their effect on plasma 17-OHCS concentrations. B. S.

In Vivo Release of Histamine From Rabbit Blood by Reserpine. Waalkes, T. P., and Weissbach, H.: Proc. Soc. Exper. Biol. & Med. **93**: 394, 1956.

Rabbits were given a single intravenous injection of reserpine. Blood specimens, taken prior to and at various intervals after the injection, were analyzed chemically for histamine and serotonin. The reduction in whole blood histamine following the injection of reserpine was similar in rate and degree to the reduction in whole blood serotonin. The histamine and serotonin values declined to a minimal level at about 20 hours, remained low until about 48

hours, and returned to normal in 5 to 7 days. The minimum histamine levels at 40 hours after reserpine injection varied from 7 to 25 per cent of the control value in the rabbits.

Previous studies demonstrated that platelet counts were essentially the same in rabbits before and 16 hours after the intravenous injection of reserpine. Since whole blood histamine and serotonin are found in platelets in the rabbit, the decrease in these substances in the blood after reserpine administration cannot be accounted for on the basis of a reduction in whole blood platelet count. Rather, a release from platelets is postulated with subsequent metabolism of both serotonin and histamine.

Platelets were isolated from rabbit whole blood drawn before and 24 hours after an intravenous injection of reserpine. Chemical analysis revealed a marked reduction in both histamine and serotonin content of the platelets following the reserpine injection. These findings support the release phenomenon hypothesis.

These and other studies suggest that reserpine is capable of liberating such potent biologically active substances as histamine, serotonin, and epinephrine from blood and tissues. Other reports have shown that histamine causes a release of catechol amines and that epinephrine causes a release of histamine. Serotonin has been shown to release histamine from tissues. Thus, these agents are possibly able to release each other from blood and tissues. Reserpine may be capable of liberating histamine, serotonin, and epinephrine primarily or, by liberating one of these, of causing a secondary release of the others. The therapeutic and side effects of reserpine may be due to the release of these compounds, their interaction, and resultant loss. B. S.

Newer Drugs for Relief of Allergic Diseases. Arbesman, C. E.: New York J. Med. **56**: 3678, 1956.

A number of the "newer" medications for the relief of asthma and allergic rhinitis were subjected to clinical trial. In a series of 139 patients treated with prednisone and prednisolone, it was found that the chief advantage of these drugs over other steroids, such as cortisone, hydrocortisone, or ACTH, was that they are less likely to cause edema and sodium retention. The chief disadvantage of prednisone and prednisolone is the relatively high incidence of gastrointestinal side effects, such as epigastric pain, nausea, cramps, diarrhea, and flare-up of dormant ulcers, which they produce.

The efficacy of "Spansules" of aminophylline was investigated in 25 asthmatic patients. Each Spansule tablet contains 4.5 grains of aminophylline and is so constituted that one-third of it dissolves rapidly, releasing the initial therapeutic dose. The remainder is coated with a digestible material and is embedded in the matrix of the tablet. As the matrix disintegrates, small coated aminophylline granules are released and exposed to the gastrointestinal secretions. The patient therefore receives hundreds of small divided doses spread evenly over an 8-hour period. It was thought that a preparation of this kind would eliminate the gastric irritation which ordinarily accompanies the oral administration of large doses of aminophylline. The results of the clinical trials with the Spansules indicated that this preparation was less efficacious than aminophylline suppositories and the problem of gastric irritation was not eliminated.

Dapanone, a bronchodilator similar to Aludrine, epinephrine, ephedrine, etc., but found in the laboratory to lack the central nervous system stimulation of the above-named drugs, was subjected to clinical trial in 26 asthmatic

patients. It was found that, although Dapanone was an efficient bronchodilator, it presented no advantage over the older preparations because of the high incidence of side effects which it produced.

Isuprel-Franol tablets, which consisted of an outer coating of Isuprel and an inner tablet, Franol (benzylephrine hydrochloride, phenobarbital, and theophylline), was investigated for its efficacy in producing immediate and prolonged relief in 33 asthmatic patients. Patients reported many side effects with this medication. It had the same effect as ephedrine compounds plus the immediate action of sublingual Isuprel.

Plimasin, a tablet containing 25 mg. of Pyribenzamine and 5 mg. of Ritalin (a stimulating drug for counteracting the soporific effects of Pyribenzamine), was tested clinically in 108 patients suffering from hay fever, perennial rhinitis, and urticaria. It was found that a number of patients who could not tolerate Pyribenzamine or other antihistaminics because of drowsiness tolerated Plimasin well. M. A.

Studies on the Capacity of Some Polysaccharides to Elicit Antibody Formation in Man. Allen, P. Z., and Kabat, E. A.: J. Exper. Med. **105**: 383, 1957.

Human volunteers were injected with various purified polysaccharides. Levan, a polysaccharide consisting chiefly of polymerized fructose, was obtained from each of four microorganism sources. These levans were found to be antigenic, producing precipitin antibody and giving rise to a wheal-erythema type of skin sensitivity. No passive transfer studies were reported. Skin reactivity occurred independently of precipitin or coprecipitin formation. Micro-quantitative precipitate analysis was carried out. The presence of fructose in the specific precipitate indicated that the antibody produced was antilevan. Structural differences among levans were discussed. Antilevan in one serum was partially precipitated by rye grass levan. Purified soluble laminarin, a neutral polysaccharide obtained from *Laminaria digitata,* unexpectedly produced precipitation with normal human sera. Apple amylopectin, maize glycogen, and two synthetic polyglucoses did not excite antibody formation in the limited number of individuals injected. E. K.

Two Types of γ-Globulin Differing in Carbohydrate Content. Müller-Eberhard, H. J., Junkel, H. G., and Franklin, E. C.: Proc. Soc. Exper. Biol. & Med. **93**: 146, 1956.

The heavy component (19 S) of normal human serum was concentrated by repeated cycling in an ultracentrifuge. Zone electrophoresis of the 19 S component revealed that it is distributed in two electrophoretic fractions with peak concentrations in the γ_1 and α_2 regions.

Different preparations of γ-globulin with varying amounts of heavy component were examined in the analytical ultracentrifuge and subjected to carbohydrate analysis. A direct relationship was found between the percentage of heavy component in the γ-globulin preparations and the carbohydrate peptide ratio. It was also found that the 19 S high molecular weight fraction of γ-globulin contained approximately 5 times as much hexose sugars as the major 7 S fraction. Furthermore, the 19 S component had a low hexosamine-hexose ratio and was relatively rich in sialic acid. Analysis of the α_2 fraction of the heavy component was found to be similar to the γ_1 fraction.

The concentration of the 19 S component in the sera of 4 patients with agammaglobulinemia was found to be one-tenth or less than that found in normal sera.

The high carbohydrate content of the 19 S group proteins which migrate in the γ-globulin region indicates that they are not simple aggregates of the main 7 S type. Immunologic studies not reported in this paper indicate that there are antigenic differences between these 2 types of γ-globulin, but that there is also considerable cross reaction. Similar antigenic relationships have been demonstrated between 19 S and 7 S components in horse sera. In human beings, the blood group antibodies, certain abnormal red cell antibodies, and part of the Wassermann antibodies are thought to be localized in the 19 S fraction of γ-globulin. There is the possibility that these antibodies are rich in carbohydrate. The markedly reduced levels of 19 S fraction in the sera of patients with agammaglobulinemia suggest further a relationship between the heavy components and antibodies. B. S.

Passive Transfer With Circulating Leukocytes of Delayed Hypersensitivity to Cat Scratch Antigen. Warwick, W. J., Page, A., and Good, R. A.: Proc. Soc. Exper. Biol. & Med. **93**: 253, 1956.

Blood was withdrawn from 3 patients who were convalescent from cat scratch disease and who demonstrated strongly positive delayed skin test reactions to cat scratch antigen. The blood was collected in silicone-coated bottles to which an anticoagulant was added. It was then allowed to stand at room temperature for 50 minutes, and then the plasma containing the white blood cells was removed and centrifuged. The supernatant plasma was then poured off and the leukocytes with an approximately equal number of admixed red cells were suspended in normal saline. The cellular suspension from each patient was then injected intramuscularly, or intramuscularly and subcutaneously, into 3 recipients. The number of viable cells transferred varied from 260,000,000 to 1,000,000,000. The recipients were children with negative skin test reactions to cat scratch antigen, whose blood groups were compatible with those of the donors. The recipients were skin tested with the antigen two days after the transfer of cells and at weekly intervals thereafter and the tests were read for induration and edema at 48 hours.

In all 3 cases, passive transfer of cat scratch disease skin hypersensitivity was successfully accomplished. The transferred skin hypersensitivity lasted from 2 to more than 4 weeks.

A convalescent patient with a strongly positive skin reaction to cat scratch antigen was bled and 150 c.c. of his plasma was injected intravenously into a recipient. The subject failed to develop a positive skin reaction to cat scratch antigen.

This is the first report of successful passive transfer of skin hypersensitivity to a disease which is presumed to be of viral etiology. B. S.

Miscellaneous

Role of Tranquilizing Drugs in Allergy. Eisenberg, B. C.: J. A. M. A. **163**: 934, 1957.

In a preliminary study, clinical observations were made on three groups of allergic patients who were receiving chlorpromazine, reserpine, or meprobamate. Patients who exhibited undue anxiety or depression or whose symptoms had failed to respond to routine allergic management were selected for this study. Chlorpromazine (Thorazine) was of some benefit to 19 of 59 such patients; meprobamate (Equanil, Miltown) helped 32 of 83 patients; and reserpine (Serpasil) improved 11 of 52 patients. These results were considered to be sufficiently encouraging to warrant further study of the effect of tranquilizing drugs in allergic diseases. M. C.

Fatalities Following Topical Application of Local Anesthetics to Mucous Membranes. Adriani, J., and Campbell, D.: J. A. M. A. **162**: 1527, 1956.

During a 15-year period there were 15 unreported deaths in the New Orleans area following the topical application of tetracaine to mucous membrane surfaces for endoscopic procedures. A review of these fatalities revealed that excessive doses of tetracaine were used, that resuscitative equipment or antidotes were not immediately available, and that novices were using the drug for the first time. Reactions with tetracaine were usually abrupt with no prodromal signs or convulsions.

The blood level of tetracaine in dogs was measured after various methods of administration. A higher blood level was obtained after topical application of the drug to the pharyngeal and nasal mucous membranes than after slow intravenous administration or subcutaneous infiltration. The absorption curve following topical application simulated the curve produced by rapid intravenous administration of the drug. Because tetracaine is so rapidly absorbed from mucous membranes, it may cause accidents because of overdosage. The author prefers cocaine as a topical anesthetic. M. C.